

apoptosis-inducing activity. The inhibition of capsid protein apoptosis-inducing activity can be monitored in many ways, including, but not limited to, use of the TUNEL (TdT-mediated dUTP-X nick end labeling) assay and monitoring of PS with annexin V.

As used herein, “injectable pharmaceutical composition” refers to pharmaceutically acceptable compositions for use in patients that are sterile, pyrogen-free, and free of any particulates. See, *Remington’s Pharmaceutical Sciences*, 18<sup>th</sup> Ed., Gennaro, ed., Mack Publishing Co., Easton, PA, 1990 and U.S.P., the standards of the U. S. Pharmacopeia, which is incorporated herein by reference.

As used herein, “pharmaceutically acceptable carrier” includes any carrier that does not itself induce a harmful effect to the individual receiving the composition. For example, a “pharmaceutically acceptable carrier” should not induce the production of antibodies harmful to the recipient. Suitable “pharmaceutically acceptable carriers” are known to those of skill in the art and are described in *Remington’s Pharmaceutical Sciences*, *supra*.

As used herein, “hyperproliferating cells” refers to cells that are growing, dividing, or proliferating at an inappropriate or non-normal time or place, and includes cells that have entered the cell cycle when they should be in G<sub>0</sub> or in a quiescent state. For example, tumor cells are included within the meaning of “hyperproliferating cells.” Diseases or conditions characterized by or associated with “hyperproliferating cells” include cancer, autoimmunity, non-malignant growths, and psoriasis.

As used herein, “treating” includes the amelioration and/or elimination of a disease or condition. The term “treating” is used in reference to individuals suffering from a disease or condition characterized by or associated with hyperproliferating cells and is also used in reference to individuals exposed to and/or infected with WNV or other viruses including *Flaviviruses* or *Pestiviruses*.

As used herein, the phrase “effective amount” in reference to treating an individual having a disease or condition, means a quantity sufficient to effectuate treatment and ameliorate and/or eliminate the disease or condition.

As used herein, the phrase “immunologically effective amount” in reference to vaccine compositions, means a quantity sufficient to induce a therapeutic or prophylactic immune response.

As used herein, the phrase “prophylactic immune response” in reference to treating an individual against infection from a virus, means an immune response that is prophylactic and protects from challenge with the virus.

As used herein, the phrase “therapeutic immune response” in reference to treating an individual infected with a virus, means an immune response that ameliorates and/or eliminates the viral infection.

As used herein, the phrase “therapeutically effective amount” in reference to the amount of a vaccine administered to an individual, means a quantity sufficient to induce a therapeutic immune response in the individual.

As used herein, the phrase “prophylactically effective amount” in reference to the amount of a vaccine administered to an individual, means a quantity sufficient to induce a prophylactic immune response in the individual.

As used herein, “individual” refers to human and non-human animals that can be treated with pharmaceutical compositions or vaccine compositions of the invention.

As used herein, the term “administering” includes, but is not limited to, intra-tumoral injection, transdermal, parenteral, subcutaneous, intra-muscular, oral, and topical delivery.

As used herein, “intra-tumoral injection” in reference to administration of pharmaceutical compositions refers to the direct introduction of the pharmaceutical composition into a tumor site by injection.

Several aspects of the invention relate to the ability of capsid protein from WNV or other viruses including *Flaviviruses* or *Pestiviruses*, or functional fragments thereof, to inhibit cell proliferation. Several aspects of the invention also relate to the ability of other viral proteins from other viruses including *Flaviviruses* or *Pestiviruses*, or functional fragments thereof, to inhibit cell proliferation. The capsid or other protein induces cells to undergo apoptosis. In some embodiments, capsid protein from WNV or other virus including *Flaviviruses* or *Pestiviruses*, or a functional fragment thereof, and/or a nucleic acid molecule that encodes it, is used in a pharmaceutical composition to treat individuals suffering from diseases characterized by or associated with undesirable cells, particularly hyperproliferating cells such as cancer. The WNV or other virus including *Flavivirus* or *Pestivirus* capsid or other protein presents a target for the interruption of a vital viral function. Accordingly, in one aspect of the invention, anti-viral and/or anti-WNV and/or anti-*Flavivirus* or anti-*Pestivirus* compounds may be identified by

identifying compounds that inhibit the apoptosis-inducing activity of WNV or other viruses including *Flaviviruses* or *Pestiviruses* capsid or other protein, or functional fragments thereof.

The present invention also relates to the use of functional fragments of WNV or other viruses including *Flaviviruses* or *Pestiviruses* capsid or other protein, and/or a nucleic acid encoding functional fragments of WNV or other viruses including *Flaviviruses* or *Pestiviruses* capsid or other protein, to induce apoptosis in cells, and to pharmaceutical compositions that comprise functional fragments of WNV or other viruses including *Flaviviruses* or *Pestiviruses* capsid or other protein, and/or a nucleic acid encoding functional fragments of WNV or other viruses including *Flaviviruses* or *Pestiviruses* capsid or other protein. As used herein, a “functional fragment” of “capsid protein from WNV or a related *Flavivirus* or *Pestivirus*” refers to a fragment of WNV or related *Flavivirus* or *Pestivirus* capsid protein which retains its ability to induce apoptosis of cells. As used herein, a “functional fragment” of “capsid or other protein from WNV or other virus including *Flavivirus* or *Pestivirus*” refers to a fragment of WNV other virus including *Flavivirus* or *Pestivirus* which retains its ability to induce apoptosis of cells. Functional fragments of WNV or other virus including *Flavivirus* or *Pestivirus* capsid or other protein are at least about 10 amino acids in length, derived from WNV or other virus including *Flavivirus* or *Pestivirus* capsid or other protein, and may comprise amino acid sequences that are not derived from the capsid or other protein from WNV or other viruses including *Flavivirus* or *Pestivirus*.

It has also been observed that a 22 amino acid residue peptide from the carboxy-terminal region of WNV Cp protein has apoptosis-inducing activity for certain embodiments of the invention. This peptide (“WNVC-P3”, also referred to herein as “Peptide 3”) is shown in Figure 10, and represents amino acid residues 90 through 110 of the WNV Cp protein. In particular, according to some embodiments of the invention, a functional fragment of WNV Cp protein includes peptide WNVC-P3, or a fragment thereof. The fragment of peptide WNVC-P3 comprises at least 3 amino acids. The fragment of peptide WNVC-P3 can be 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or 21 amino acid residues in length. Peptide WNVC-P3 of WNV Cp protein, a fragment thereof, a fragment of Cp protein that includes peptide WNVC-P3 or fragment thereof, the Cp protein or a fusion protein, comprising Cp protein sequences and non-Cp protein sequences, can all be tested to determine whether they possess the apoptotic function of the wild type Cp protein.